GM

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/833,675	04/13/2001	Thomas Weimer	06478.1454-00	2127

22852 7590 06/25/2004

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
1300 I STREET, NW
WASHINGTON, DC 20005

EXAMINER	
LY, CHEYNE D	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 06/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/833,675	WEIMER, THOMAS	
	Examiner	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-34* is/are pending in the application.

4a) Of the above claim(s) *26-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *10-34* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/5/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's arguments filed April 07, 2004 have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

2. Claims 10-25 are examined on the merits.

IDS

3. The European Search Report, Application No. 01107541.3-1222, has not been considered because said report does not have a publication date.

CLAIM REJECTIONS - 35 U.S.C. § 112, SECOND PARAGRAPH

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 10-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. This rejection is maintained with respect to Claims 10-25, as recited in the previous office action mailed October 08, 2003.

RESPONSE TO ARGUMENTS

7. Applicant argues that the phrase "mutually overlapping" is well known to those of skill in the art and thus is not vague and indefinite. Applicant cites the documents listed in the IDS, filed April 05, 2004, to support that the phrase "mutually overlapping" is used to describe

single-stranded "oligonucleotide sequence fragments." Further, Applicant cites the instant specification (page 3, lines 20-24), which recites sequence fragments comprising 30-50 bases not base pairs as support that the instant claims are not vague and indefinite. The above arguments have been fully considered and found to be unpersuasive as discussed below.

8. It is acknowledged that it is well known in the art that the term "oligonucleotide" refers to singled-stranded sequence. However, the instant elected claims are directed to "oligonucleotide sequences for use in amplifying a target nucleic acid sequence." It is well known in the art that amplification reactions comprising of primers (oligonucleotide fragments) form primer dimers (double stranded) nucleotide sequences (Erlich 1992). Therefore, the phrase "mutually overlapping", as being used to describe the "oligonucleotide sequence fragments" in the instant claims, is vague and indefinite because it is unclear as to whether the overlapping DNA molecules are single or double stranded.

9. Further, Applicant argues that the mutually overlapping oligonucleotide sequence fragments refers to fragments that have identical sequences in the "overlapped" sequence, and said overlapped sequences share an identical portion. Applicant's argument has been found to be unpersuasive because the criteria for determining "mutually overlapping oligonucleotide sequence fragments" has not been set forth in the instant application. What criteria are being used to determine that one sequence mutually overlaps with another sequence? Are oligonucleotide sequence fragments that have 2-nucleotide sequence identity "mutually overlapping"? How many nucleotide identities are required for oligonucleotide sequence fragments to be considered as "mutually overlapping"? Claims 11, 12, 17-19, 21-25 are rejected due to being directly or indirectly dependent from claim 10 or 20.

CLAIM REJECTIONS - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 10-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neri et al. (US 6,194,149 B1) taken with Chee et al. (US 5,837,832 A) in view of Tureci et al. (US 6,214,983 B1).

12. This rejection is maintained with respect to Claims 10-25, as recited in the previous office action mailed October 08, 2003.

RESPONSE TO ARGUMENTS

13. Applicant argues that "the Examiner has not met his burden for establishing a *prima facie* case of obviousness" because said examiner has failed to show that all elements of the present invention are present in the cited references. Applicant's arguments have been fully considered and found to be unpersuasive as discussed below.

14. Specific to the argument that Neri et al. does not disclose the limitations of steps a), b), and c) of claim 10, Neri et al. discloses a method of identifying oligonucleotides for performing target-dependent reactions. The method of Neri et al. comprises selecting the target nucleic acid sequence, generating overlapping fragments to a conserved region (column 46, lines 50-60) and determining the similarity of the fragments by an alignment (Figures 18 a-d). The primers are employed for polymerase chain reactions (PCR) (column

54, lines 61-67 to column 55, lines 1-15). The citation above fully supports that Neri et al. discloses the limitations of claim 10, steps a) and c).

15. It has been acknowledged that Neri et al. does not disclose all the limitations of claim 10, step b). The deficiency of Neri et al. has been addressed by the combination of Chee et al. as previously applied and set forth in the previous Office Action, mailed October 08, 2003. It is re-iterated that Chee et al. discloses a method for identifying heterologous oligonucleotide sequences wherein target fragmentation is performed followed by target DNA amplified by PCR with primers (column 23, lines 45-67 to column 24, lines 1-4). The said method provides redundant confirmation of conserved HIV RT and other gene sequences, and the probes on will be tile through with overlap (column 25, lines 3-7 and Figure 1), as in instant claim 10, step b).

16. Applicant further argues that the Examiner has mischaracterized the disclosure of Chee et al. because said disclosure does not support the limitation of "identifying heterologous nucleotide sequences" in the elected claims. The method of Chee et al. is directed to determining whether a target nucleic acid has a nucleotide sequence identical to or different from a specific reference sequence. It is re-iterated that Chee et al. discloses a method for identifying heterologous oligonucleotide sequences wherein target fragmentation is performed followed by target DNA amplified by PCR with primers (column 23, lines 45-67 to column 24, lines 1-4). The said method provides redundant confirmation of conserved HIV RT and other gene sequences, and the probes on will be tile through with overlap (column 25, lines 3-7 and Figure 1), as in instant claim 10 step b).

17. It is the combination of the disclosures of Neri et al. and Chee et al. as a whole which fully discloses the limitations of claim 10, steps a), b), and c).

18. Applicant argues that Tureci et al. does not disclose any limitations in claim 10. Further, Applicant argues that the database search described in Tureci et al. is different from the search for heterologous sequences in the instant invention. Applicant's argument has been fully considered and found to be unpersuasive because Tureci et al. discloses a method comprising an electronic search of the GenBank database to identify known nucleic acid molecules and said search yield non-homologous (heterologous sequences). The results of the said search were used to generate heterologous primers (oligonucleotide sequences). (column 4, lines 9-27).

19. Specific to Applicant's argument that the instant claimed invention uses "mutually overlapping fragments as query fragments, rather than the functional criteria used in Tureci et al., Applicant's argument has been fully considered and found to be unpersuasive. Consistent with the scope the claim 19 which recites oligonucleotide sequences are identified in a DNA sequence database, the GenBank search according to Tureci et al. is performed in a DNA sequence database. Further, the sequence search is performed via BLAST search of the DBEST database (column 4, lines 18-19), as in instant claim 19.

20. It is the combination of the disclosures of Neri et al., Chee et al., and Tureci et al. as a whole which fully discloses the limitations of claim 19.

21. Applicant argues that the "only support the Examiner mentions for a motivation to combine is that Neri et al., Chee et al., and Tureci et al. are all in the fields relating to nucleic acids." Applicant's argument has been fully considered and found to be unpersuasive

because Neri et al. discloses improvements via useful tools for rapidly analyzing nucleic acid structure as directed to basic and clinical research, and diagnostics. It is noted that the disclosures of Neri et al., Chee et al., and Tureci et al. are in the same field of endeavor such as methods directed to nucleic acids. However, the improvement of Neri et al. is directed to useful tools for rapidly analyzing nucleic acid structure as directed to basic and clinical research, and diagnostics. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated to partake the improvements disclosed by Neri et al. to improve said method with the disclosure of Chee et al. and Tureci et al.

22. Applicant argues that Applicant still fails to see the identity of Figure 18(a) in Neri et al. and SEQ ID NO. 1. Applicant's argument has been fully considered and found to be unpersuasive because consistent with the scope of claims 12-17, a nucleotide sequence CCC of Figure 18(a) could reasonably be construed as an oligonucleotide sequence from SEQ ID NO. 1 of this instant application.

REJECTION RE-ITERATED

23. Neri et al. discloses a method of identifying oligonucleotides for performing target-dependent reactions. The method of Neri et al. comprises selecting the target nucleic acid sequence, generating overlapping fragments to a conserved region (column 46, lines 50-60) and determining the similarity of the fragments by an alignment (Figures 18 a-d), as in claims 10 and 11.

24. Figure 18 a discloses an oligonucleotide from 70 to 263 of HCV 1a with a nucleotide sequence CCC that is identical to the oligonucleotide sequence of SEQ ID NO. 1 of this instant application, as in claims 12-17.

25. A record reference library of genetic fingerprints comprising nucleic acids is generated with the method of Neri et al. (column 12, lines 36-48), as in claim 18.

26. Oligonucleotide probes comprise of universal bases (column 10, lines 20-27) and which may include inosine (column 26, lines 11-18). Further, the probes having mismatches are used for more sensitive detection method (column 50, example 1), as claims 20 and 21.

27. Probes are used for hybridization analysis in HCV genotyping (column 53, Example 3), as in claim 22.

28. The primers are employed for polymerase chain reactions (PCR) (column 54, lines 61-67 to column 55, lines 1-15), as in claims 23-25.

29. However, Neri et al. does not disclose the limitations wherein the target nucleic acid is fragmented to produce overlapping fragments as in instant claim 10 step b).

30. Chee et al. discloses a method for identifying heterologous oligonucleotide sequences wherein target fragmentation is performed followed by target DNA amplified by PCR with primers (column 23, lines 45-67 to column 24, lines 1-4). The said method provides redundant confirmation of conserved HIV RT and other gene sequences, and the probes on will be tile through with overlap (column 25, lines 3-7 and Figure 1), as in instant claim 10 step b).

31. However, Neri et al. and Chee et al. do not disclose the oligonucleotide sequences as being identified in a DNA sequence library, as in claim 19.

32. Tureci et al. discloses a method comprising an electronic search of the GenBank database to identify know nucleic acid molecules and the results of the said search was used to generate primers (column 4, lines 9-27), as in claim 19.

33. Neri et al. discloses improvements via useful tools for rapidly analyzing nucleic acid structure as directed to basic and clinical research, and diagnostics. While, Chee et al. discloses a diagnostic method for analyzing nucleic acid molecules (column 1, lines 19-24) and Tureci et al. discloses a method for analyzing nucleic acid for diagnostics uses (Abstract etc.). Therefore, the improvements disclosed by Neri et al. is directly applicable to the method for analyzing nucleotide molecules for diagnostic uses as taught by Chee et al. and Tureci et al.

34. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated to partake the improvements disclosed by Neri et al. to improve said method with the disclosure of Chee et al. and Tureci et al. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to practice method of identifying oligonucleotides for performing target-dependent reactions with the step of target fragmentation and a sequence library as taught by Neri et al., Chee et al. and Tureci et al.

CONCLUSION

35. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

36. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to

37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

37. This application contains claims 26-34 drawn to an invention nonelected with traverse, April 25, 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

38. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

39. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

40. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

41. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

42. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

C. Dune Ly
6/20/04

Ardin H. Marschel 6/22/04
ARDIN H. MARSCHEL
PRIMARY EXAMINER